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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/173,821 | 10/16/98 | RUDLAND | P 32040PCTUSA- |

HM22/0515

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| EXAMINER | |
|---|---|
| KAUSHAL,S | |
| **ART UNIT** | **PAPER NUMBER** |
| 1633 | 11 |

**DATE MAILED:** 05/15/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/173,821 | Rudland et al |
| **Examiner** | **Group Art Unit** |
| SUMESH KAUSHAL | 1633 |

☒ Responsive to communication(s) filed on *Feb 23, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claim**

☒ Claim(s) *1, 3, 4, 6-9, 13, and 15-29* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3, 4, 6-9, 13, and 15-29* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*— SEE OFFICE ACTION ON THE FOLLOWING PAGES —*

## DETAILED ACTION

The applicant's response filed on Paper No.9, filed 02/23/00 has been fully considered but they are not persuasive for the reasons set forth in the earlier office action (Paper No.7, 08/17/99) and new grounds of rejections below. Claims 2, 5, 10-12 and 14 are canceled. Claims 1, 3-4, 6-8, 13 and 15-24 are amended. Newly filed claims 25-29 are entered. Claims 1, 3-4, 6-9 and 15-29 are pending in this application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Claim Objections*

1. Claims 19 and 20 are objected to under 37 CFR 1.75© as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 19 and 20 have not been further treated on the merits.

### *Claim Rejections - 35 USC § 112*

Claims 1, 3-4, 13, 15-17, 19-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for i) a cell line derived from a transgenic rat comprising: B2LT1 rat mammary cells (MMTV-SV40tsA58) and NF2 rat brain cells (NS-LtsA58) ii) transgenic

rats comprising: MMTVLTR-TGFα and MMTVLTR-C-erb-B-2, does not reasonably provide enablement for any and all transgenic cell lines and/or transgenic rats comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention **commensurate in scope** with these claims.

2. Applicant's arguments filed 02/23/00, page 8, para. 3, have been fully considered. Applicant's argument that recitation of mammal to rat and deletion of reference to mammary, liver and kidney cell line obviate this rejection is not persuasive because the instant claims after the amendment read upon a transgenic rat comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters. However, the instant specification is only enabled for i) cell line derived from transgenic rat comprising: B2LT1 rat mammary cells (MMTV-SV40tsA58) and NF2 rat brain cells (NS-LtsA58) ii) transgenic rats comprising: MMTVLTR-TGFα and MMTVLTR-C-erb-B-2. It is important to note that, the scope of the claims include rats encoding any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters. As stated in earlier official action (page 6, para. 1), the transgene expression and physiological consequences of transgene products are not always accurately predictable because cis elements are controlled differently by various transacting factors in the genome of an animal. Therefore, the skilled artisan at the time of filing would be lacking a reasonable expectation of success for making neuronal transgenic cell lines derived from transgenic rat(s), comprising any and all conditional transforming genes or immortalizing genes or cell cycle affecting genes and cell type specific promoters, without having to engage in an undue amount of experimentation for the breadth of the claims.

*Claim Rejections - 35 USC § 103*

3. Claims 1, 3-4, 6-9, 13, 15-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noble at al (WO 91/13150, 1991), Stocklin et al (J. Cell Bio. 122(1):199-208, 1993), Moses JH (Br. J. Cancer. 69(21):1, 1994) in view of Reeben et al (Biochem. Biophy. Res. Com. 192(2):465-470, 1993) and Yazdanbakhsh et al (Nuc. Acid. Res. 21(3):455-61, 1993) in view of Leder et al (US Pat No. 5087571, 1992) and further in view of Hammer et al (US Pat. No. 5489742, 1996)

Noble et al teaches transgenic animals and cell lines from any cell type of the animal body, wherein the cell line comprises **SV40tsA58** immortalizing gene (fig-1; page 34, line 1-20, page 35-40, page 50, line 19, page 53, line 22, page 56, line 16, page 59, example-3, page 61 example-4 page 64, example-5 page 69, example-6, page 74, example-7).

Stocklin et al teaches a transgenic mice wherein the human **c-erbB-2** is operably linked to MMTV enhancer/promoter sequence wherein the transgene is expressed in kidney, lung, mammary, muscle, spleen, brain and liver cells (page 200, col.2 para.5, page 201, fig-1, col.2 para 2-3, page 202, table-II).

Moses teaches a tarnsgenic mice expressing a gene encoding **hu TGF-a** under the control of MMTV enhancer/promoter (page 1, s1).

However, Noble et al, Stocklin et al and Mosses does not teach the use of **human neurofilament (NF-L) promoter** to derive the expression of **SV40tsA58, c-erbB-2 and TGF-a** genes.

Yazdanbakhsh et al teaches **human neurofilament (NF-L) promoter** which regulates neuronal-specific expression (page 455, abstract).

Leder et al teaches method of providing a cell line from a transgenic mice encoding a transforming oncogne operably linked to mammary specific promoter MMTVLTR (col.4 line 13-22, col.9 line 11-20). Leder et al also teaches the use of transgenic mice for testing a material suspected of being a carcinogen (col.8 line 50-68). The cited art also teaches a method of testing a material for its ability to confer protection against the development of neoplasms using transgenic animals (col.9 line 1-9).

Although the combination of Noble et al, Stocklin et al, Mosses, Yazdanbakhsh et al Leder et al teaches a transgenic mice and/or cell line and a method of screening carcinogens, wherein in the transgenic cell the human neurofilament (NF-L) promoter to derive the expression of SV40tsA58, c-erbB-2 and TGF-a genes, it does not teach the making of a transgenic rat encoding the same.

Hammer et al teaches a method for producing transgenic rats, by super ovulating a female rat by continuous supply of FSH hormone using a mini-pump and introduction of the selected transgene into the fertilized eggs (col.15 line 60-67, col.1, line 1-17).

Thus, it would have been obvious to one ordinary skill in the art at the time of filing to have substituted the transgenic mice (encoding human neurofilament promoter which derives the expression of SV40tsA58, c-erbB-2 or TGF-a gene) as taught by Noble et al, Stocklin et al, Mosses and Yazdanbakhsh et al with a transgenic rat as taught by Hammer et al. It would have been further obvious to test a material suspected of being carcinogen a transgenic rat as taught by Leder. One would have been motivated to do this because rats are widely used in biomedical research, and in

addition to transgenic mice, a transgenic rat model would provide a two fold experimental approach for the same transgene.

***Conclusion***

No claims are allowed.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-2035. Any inquiry of a general nature or relating to the status

of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

S. Kaushal, AU 1633

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